REMARKS

Reconsideration of this Application is respectfully requested.

As a preliminary matter, Applicants would like to thank the Examiner for the courtesy of the telephone interview regarding this case.

Claims 1, 4-8, 10-11, 14-18, 20-23, 41, 47, 69, 95-99 and 100-101 are currently pending. Claims 2-3, 9, 12-13, 19, 24-40, 42-46, 48-68, 70-94 and 102-103 have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of the canceled claims in one or more divisional or continuation applications.

Claims 1, 4, 5-6, 10, 15-16, 18, 20-21, 41, 95-97 and 100-101 have been amended. No new matter is added.

Support for the amending language may be found in the claims as filed and in the specification at least as follows:

SEQ ID NO:32 (a preferred "complete" TPL nucleic acid molecule containing complete TPL exons 1, 2 and 3 with adenovirus intron 1 inserted between exons 1 and 2). [paragraph 0158 of the published application; Claim 14]

SEQ ID NO:26 (a partial TPL exon containing partial TPL exon 1 and complete TPL exons 2 and 3 in that order. [paragraph 0158 of the published application; Claim 14]

SEQ ID NO:8 (the TPL nucleotide sequence in pCLF bordered by BamHI/BglII 5' and 3' sites at respective nucleotide positions 907-912 to 1228-1233. [paragraph 0279 of the published application; Claims 100 and 101]

The nucleic acid sequence of complementing plasmids are shown in SEQ ID NO: 43 for pDV60, SEQ ID NO: 44 for pDV67 and SEQ ID NO: 47 for pDV69, SEQ ID NO: 64 for pDV80 and SEQ ID NO: 65 for pDV90. [paragraph 166 of the published application; Claims 10 and 18]

In the Office Action dated June 2, 2004, the Examiner set forth a number of grounds for rejection. These grounds are addressed individually and in detail below.

Double Patenting Rejection

Claims 41, 47 and 95-97 stand provisionally rejected under the judicially-created doctrine of obviousness-type double patenting over Claims 57, 58, 60, 65 and 66 of co-pending Application No. 09/795,292 for the reasons set forth on page 4 of the June 2, 2004 Office Action.

Applicants respectfully submit that the present claims are not obvious in view of the claims of the cited patent. However, in order to further prosecution, filing of a terminal disclaimer will be considered upon indication of otherwise allowable subject matter.

Rejection under 35 U.S.C. § 112, second paragraph.

Claims 100 and 101 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention for the reasons set forth on page 5 of the June 2, 2004 Office Action. Claims 100 and 101 have been amended such that both claims ultimately depend from Claim 1, which recites the features of a sequence of nucleotides encoding a particular TPL, SEQ ID NO:8.

Applicants respectfully submit that the grounds for the 35 U.S.C. § 112, second paragraph rejections have been obviated by the amendments described above. Withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Rejection under 35 U.S.C. §112, first paragraph, enablement.

Claims 9, 18, 100, 102 and 103 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement.

The Office Action maintains that plasmids pCLF, pDV60, pDV67, pDV69, pDV80 and pDV90 are required elements of the claims and as such must be known and readily available to the public or be obtainable by a repeatable method set forth in the specification. The Office Action further states that a statement of deposit of the plasmids may satisfy the enablement requirement.

Claims 9, 102 and 103 have been cancelled. Claim 18 has been amended to recite the corresponding SEQ ID NOs for each plasmid recited in the claim. Claim 100 recites SEQ ID NO:8 and does not refer to plasmid pCLF.

The first paragraph of 35 U.S.C. § 112 requires that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention. Although the statute does not say so, enablement requires that the specification teach those in the art to make and use the invention without undue experimentation (e.g., In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir., 1991). An invention is enabled even though the disclosure may require some routine experimentation to practice the invention. Hybritech Inc, V. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986).

In accordance with the accepted standards of enablement set forth above, an invention is enabled if one skilled in the art could make and use the claimed invention without undue experimentation. Deposit of biological materials is not necessary if the materials, or starting materials, are known and readily available to the public, or obtainable by a repeatable method set forth in the specification. For plasmids pDV60, pDV67, pDV69, pDV80 and pDV90, the

complete nucleotide sequences are recited in the current claims and provided in the Sequence Listing as SEQ ID NOs. 43, 44, 47, 64 and 65, respectively.

Applicants submit that one of skill in the art could make and use the subject matter of Claims 18 and 100 based on the specific sequence information provided in the claims.

In view of the above amendments and remarks, withdrawal of the rejection under 35 U.S.C. § 112 is respectfully requested.

Rejection under 35 U.S.C. § 102(b).

Claims 1, 2 and 11 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Logan et al. (Proc. Natl. Acad. Sci. USA, 81:3655-3659 (1984)). The Office Action maintains that Logan et al. anticipates a nucleic acid molecule comprising two TPL exons from the same adenovirus in non-native order. To support this assertion, the Office Action points to the "sub 360-L1,3" construct set forth in Figure 1 of Logan et al., which allegedly describes a TPL leader sequence containing TPL exon 1 operatively linked to TPL exon 3, wherein TPL exons 1 and 3 are from the same adenovirus.

For anticipation under 35 U.S.C. § 102, the reference "must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present." (MPEP §706.02). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Claim 2 has been cancelled. Claim 1 as amended herein is directed to an isolated nucleic acid molecule containing a sequence of nucleotides encoding an adenovirus tripartite leader (TPL), wherein the TPL-encoding sequence of nucleotides comprises: (a) first and

second different TPL exons, wherein the different TPL exons are from different adenoviruses, (b) an intron between exons of the TPL or (c) first, second and third same or different TPL exons, wherein, at least two of the different TPL exons are from different adenoviruses; and the TPL exons are selected from the group consisting of complete TPL exon 1, complete TPL exon 2 and complete TPL exon 3. Logan et al. does not describe a sequence of nucleotides encoding an adenovirus TPL which includes TPL exons from different adenoviruses (a); an adenovirus TPL that has an intron between exons (b); or first, second and third TPL exons (c).

Claim 11 is directed to a plasmid that contains the nucleic acid molecule of claim 1.

Logan et al. does not teach all the features of Claim 1 or Claim 11 which depends therefrom. Hence there is no anticipation and the rejection under 35 U.S.C. § 102 should be withdrawn.

Rejection under 35 U.S.C. §103(a).

Claim 4 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Logan et al. in view of Hodges et al. (Molecular Physiology 48:905-918 (1995)). The Office Action alleges that it would have been obvious to insert the adenovirus intron 1 allegedly taught by Hodges et al. into the TPL construct allegedly taught by Logan et al., to arrive at the claimed subject matter.

To establish a *prima facie* case of obviousness the prior art reference (or references when combined) must teach or suggest all of the claim limitations. In re Vaeck, 20 USPQ2d 1438 (Fed. Cir. 1991) and MPEP § 2142.

Claim 4 depends from Claim 1. For the reasons set forth above, Logan et al. does not teach or suggest the features of Claim 1, namely a sequence of nucleotides encoding an

adenovirus TPL which includes TPL exons from different adenoviruses (a); an adenovirus TPL that has an intron between exons (b); or first, second and third TPL exons (c).

The adenovirus intron 1 allegedly taught by Hodges et al. does not compensate for the lack of disclosure in Logan et al. with respect to the claimed TPL.

Hence, the cited references taken alone or in combination do not teach or suggest the limitations of Claim 4 and the rejection under 35 U.S.C. § 103(a) should therefore be withdrawn.

Claims 12, 13, 15-17, 20-23, 41, 47, 69 and 95-97 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Logan et al., or Sheay et al. (Biotechniques 15(5):856-862 (1993)) or Kaufman (Proc. Natl. Acad. Sci. U.S.A. 82:689-693 (1985)), in view of Curiel (U.S. Pat. No. 5,871,727) and Caravokyri et al. (J. Virology 69:6627-6633 (1995)). The Office Action alleges that Logan et al., Sheay et al. and Kaufman teach adenovirus TPL sequences, Curiel teaches a plasmid encoding a chimeric fiber protein, and Caravokyri et al. teaches packaging cell lines containing nucleotide sequences that complement pIX-deficient adenoviruses under the control of an inducible promoter.

The Office Action concludes that it would have been obvious to one of ordinary skill in the art at the time the instant application was filed to have combined the TPL constructs allegedly taught by Logan et al., Sheay et al. or Kaufman with the chimeric adenovirus fiber gene of Curiel et al. to generate a plasmid and further introduce the plasmid into a packaging cell line allegedly taught by Carvokyri et al., to arrive at the claimed subject matter.

Claims 12 and 13 have been cancelled. Current Claims 15-17, 20-23, 41, 47, 69 and 95-97, all depend from Claim 14. Claim 14 recites an adenovirus vector packaging cell line, comprising an adenovirus tripartite leader (TPL) nucleotide sequence, wherein the TPL sequence comprises a complete TPL exon 1 having the nucleotide sequence of SEQ ID NO: 32 or a partial TPL exon 1 having the nucleotide of SEQ ID NO: 26. None of Logan et al.,

Sheay et al. or Kaufman teach or suggest the particular TPL exon 1 sequences recited in SEQ ID NO: 32 or SEQ ID NO: 26. Curiel et al., directed to fiber variants to generate adenoviral vectors with altered tropism, does not cure the deficiencies of Logan et al., Sheay et al., or Kaufman, alone or in combination. Caravokyri et al, teaches a packaging cell line that complements an adenovirus by expression of a plasmid containing polypeptide IX. Similarly, Caravokyri et al. does not cure the deficiencies of Logan et al., Sheay et al., Kaufman, or Curiel et al., alone or in combination.

It follows that a combination of the cited references does not teach or suggest all of the limitations of Claim 14 and claims dependent thereon. Therefore, a *prima facie* case of obviousness has not been established and the rejection should be withdrawn.

Claims 98 and 99 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Logan et al., or Sheay et al. or Kaufman, in view of Curiel, Caravokyri et al., and Branellec et al. (U.S. Pat. No. 6,410,011). The Office Action alleges that the teachings of Branellec et al. regarding a suicide gene would have been obvious to combine with the teachings of Logan et al., or Sheay et al. or Kaufman, and Curiel and Caravokyri et al. as set forth above.

Current Claims 98 and 99 depend from Claim 95 which depends from Claim 14. Claim 14 recites an adenovirus vector packaging cell line, comprising an adenovirus tripartite leader (TPL) nucleotide sequence, wherein the TPL sequence comprises a complete TPL exon 1 having the nucleotide sequence of SEQ ID NO: 32 or a partial TPL exon 1 having the nucleotide of SEQ ID NO: 26.

Logan et al., or Sheay et al., Kaufman, Curiel and Caravokyri et al. are described above. Branellec et al. is directed to adenoviral vectors containing a recombinant suicide gene, and similar to Curiel and Caravokyri et al. does not cure the deficiencies of Logan et al., or Sheay et al., Kaufman with respect to a complete TPL exon 1 having the nucleotide

sequence of SEQ ID NO: 32 or a partial TPL exon 1 having the nucleotide of SEQ ID NO: 26.

It follows that the cited references, alone or in combination, do not teach or suggest the claimed subject matter and the rejection should be withdrawn.

Conclusions

The Examiner is respectfully requested to enter the above amendments before commencement of substantive examination. If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to contact Applicants' counsel, Linda Judge at (415) 836-2586.

Respectfully submitted,

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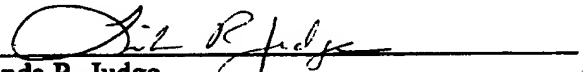

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